

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

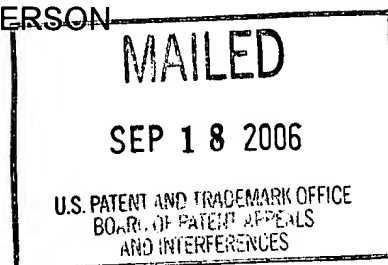
## UNITED STATES PATENT AND TRADEMARK OFFICE

### BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte PREETI LAL, NEIL C. CORLEY,  
KARL J. GUEGLER, and CHANDRA PATTERSON

Appeal No. 2006-1035  
Application No. 09/925,140

ON BRIEF



Before SCHEINER, GRIMES, and LEOVITZ, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

#### DECISION ON APPEAL

This appeal involves claims to a polynucleotide encoding, among other things, a "naturally occurring amino acid sequence at least 90% identical" to SEQ ID NO:1. The examiner has rejected the claims as nonenabled and lacking adequate written description. We have jurisdiction under 35 U.S.C. § 134. We affirm both rejections.

#### Background

"Serine dehydratase (SDH) is an enzyme involved in gluconeogenesis, the formation of glucose . . . from amino acids and certain types of fat. . . . SDH converts serine to pyruvate and  $\text{NH}_4^+$ . . . . A variety of SDHs have been observed in organisms ranging from bacteria to vertebrates. A motif which interacts with SDH's pyridoxal

5'-phosphate cofactor in several B6 enzymes is considered characteristic of SDH."

Specification, page 1.

The specification discloses a "human serine dehydratase homolog (SDHH)," having the amino acid sequence shown in SEQ ID NO:1. Page 15, lines 1-2 and 11-12. "SDHH is 329 amino acids in length and . . . has the serine/threonine dehydratase pyridoxal-phosphate attachment site at E39. . . . SDHH and rat liver serine dehydratase share 53.2% identity, and SDHH and human liver serine dehydratase share 56.7% identity." Page 15, lines 12-18.

### Discussion

#### 1. Claim construction

Claims 3-7, 9, 11, and 12 are on appeal. Claims 1, 2, 8, 10, 13-18, 27, and 28 are also pending but have been withdrawn from consideration by the examiner.

The claims stand or fall together. See the Appeal Brief, page 3. We will focus on claim 3, which is representative and reads as follows:

3. An isolated polynucleotide encoding a polypeptide selected from the group consisting of:

- a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 1,
- b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid [sequence] of SEQ ID NO: 1,
- c) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO: 1, wherein said biologically active fragment has serine dehydratase activity, and
- d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO: 1, wherein said immunogenic fragment generates an antibody that specifically binds to SEQ ID NO: 1.

The rejections on appeal focus on part (b) of the claim: polynucleotides encoding “a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid [sequence] of SEQ ID NO:1.”

## 2. Enablement

The examiner rejected claims 3-7, 9, 11, and 12 under 35 U.S.C. § 112, first paragraph, on the basis that the specification does not provide an enabling disclosure with respect to polynucleotides encoding an amino acid sequence at least 90% identical to SEQ ID NO:1. See the Examiner’s Answer, pages 3-4. The examiner noted that claim 3 is not limited to polynucleotides encoding polypeptides that have the activity disclosed in the specification for SEQ ID NO:1. Id., page 4.

The examiner reasoned that “even a small difference between sequences could render substantial differences between the activities of the proteins.” Id., page 5. As supporting evidence, the examiner cited:

- Burgess,<sup>1</sup> as teaching that “the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of . . . biological activity”;
- Lazar,<sup>2</sup> as teaching that the activity of TGF- $\alpha$  was not affected by replacing the aspartic acid at position 47 with asparagine, but replacing it with serine or glutamic acid sharply reduced biological activity;
- Schwartz,<sup>3</sup> as teaching that “[r]eplacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist”; and

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<sup>1</sup> Burgess et al., “Possible dissociation of the heparin-binding and mitogenic activities of heparin-binding (acidic fibroblast) growth factor-1 from its receptor-binding activities by site-directed mutagenesis of a single lysine residue,” Journal of Cell Biology, Vol. 111, pp. 2129-2138 (1990)

<sup>2</sup> Lazar et al., “Transforming growth factor  $\alpha$ : Mutation of aspartic acid 47 and leucine 48 results in different biological activities,” Molecular and Cellular Biology, Vol. 8, pp. 1247-1252 (1988)

<sup>3</sup> Schwartz et al., “A superactive insulin: [B10-Aspartic acid]insulin (human),” Proc. Natl. Acad. Sci. USA, Vol. 84, pp. 6408-6411 (1987)

- Lin,<sup>4</sup> as teaching that “[r]emoval of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to . . . activate adenylate cyclase.”

Id.

The examiner concluded that

one skill[ed] in the art would realize that a sequence that is 90% identical to SEQ ID NO:1 would not necessarily have the activity of SEQ ID NO:1 and therefore would not function as SEQ ID NO:1. . . . In view of the lack of predictability in the art, lack of guidance, and lack of examples, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Id., page 6.

Appellants have presented no evidence or reasoning to rebut the examiner’s position that many of the species encompassed by part (b) of claim 3 are likely to lack the function ascribed in the specification to SDHH. Rather, Appellants argue that the claimed polynucleotides are useful even if they encode inactive polypeptides: “[T]he claims are to polynucleotides, not the polypeptides they encode, and therefore it is the use of the polynucleotides that is relevant. . . . The specification recites many instances where a polynucleotide may be used, . . . whether or not th[e] encoded polypeptides had enzymatic activity.” Appeal Brief, page 5.

Appellants argue that the claimed polynucleotides can be used “in assays to detect the presence of metabolism disorders or cancer,” (id.), “to detect and quantitate gene expression in biopsied tissues in which expression of SDHH may be correlated with disease” (id.), as probes for detecting related sequences (id., page 6), in

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<sup>4</sup> Lin et al., “Structure-function relationships in glucagon: Properties of highly purified des-His<sup>1</sup>, monoiodo-, and [des-Asn<sup>28</sup>, Thr<sup>29</sup>](homoserine lactone<sup>27</sup>)-glucagon,” Biochemistry, Vol. 14, pp. 1559-1563 (1975)

microarrays to detect gene “variants, mutations and polymorphisms” (id.), or to carry out expression profiling in connection with toxicology testing (id., pages 6-8).

We agree with the examiner that the specification does not provide adequate guidance to enable those skilled in the art to make and use the claimed polynucleotides that encode a naturally occurring amino acid sequence at least 90% identical to SEQ ID NO:1. The examiner has provided evidence that even slight changes in the amino acid sequence of a protein can have large effects on the activity of the protein. Appellants have provided no evidence, or even sound reasoning, to show the contrary. Thus, a preponderance of the evidence of record supports the examiner’s position that many of the species encompassed by part (b) of claim 3 will lack the activity of SDHH. The specification does not enable those skilled in the art to use polynucleotides encoding inactive SDHH variants without undue experimentation.

The uses that can be relied on to meet the how-to-use provision of § 112 must also satisfy the utility requirement of § 101. See In re Fisher, 421 F.3d 1365, 1378, 76 USPQ2d 1225, 1235 (Fed. Cir. 2005) (“It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101.”). See also In re Kirk, 376 F.2d 936, 942, 153 USPQ 48, 53 (CCPA 1967) (“[S]urely Congress intended § 112 to pre-suppose full satisfaction of the requirements of § 101. Necessarily, compliance with § 112 requires a description of how to use presently useful inventions, otherwise an applicant would anomalously be required to teach how to use a useless invention.”).

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA. See In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The Fisher court interpreted Brenner v. Manson,

383 U.S. 519, 148 USPQ 689 (1966), as rejecting a “de minimis view of utility.” 421 F.3d at 1370, 76 USPQ2d at 1229. The Fisher court held that § 101 requires a utility that is both substantial and specific. Id. at 1371, 76 USPQ2d at 1229. The court held that disclosing a substantial utility means “show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the ‘substantial’ utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.” Id., 76 USPQ2d at 1230.

The court held that a specific utility is “a use which is not so vague as to be meaningless.” Id. In other words, “in addition to providing a ‘substantial’ utility, an asserted use must show that that claimed invention can be used to provide a well-defined and particular benefit to the public.” Id.

The Fisher court held that the uses asserted by the applicant in that case were neither substantial nor specific. The uses were not substantial because “all of Fisher’s asserted uses represent merely hypothetical possibilities, objectives which the claimed ESTs, or any EST for that matter, could possibly achieve, but none for which they have been used in the real world.” Id. at 1373, 76 USPQ2d at 1231. “Consequently, because Fisher failed to prove that its claimed ESTs can be successfully used in the seven ways disclosed in the ‘643 application, we have no choice but to conclude that the claimed ESTs do not have a ‘substantial’ utility under § 101.” Id. at 1374, 76 USPQ2d at 1232.

“Furthermore, Fisher’s seven asserted uses are plainly not ‘specific.’ Any EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses. . . . Nothing about Fisher’s seven alleged uses set the five claimed

ESTs apart from the more than 32,000 ESTs disclosed in the '643 application or indeed from any EST derived from any organism. Accordingly, we conclude that Fisher has only disclosed general uses for its claimed ESTs, not specific ones that satisfy § 101." Id.

In this case, Appellants argue that those skilled in the art could have used polynucleotides encoding inactive SDHH variants in hybridization assays to detect and quantitate gene expression, to detect related sequences or polymorphisms, or to carry out expression profiling in connection with toxicology testing. Appeal Brief, pages 5-8.

We do not agree that using the claimed polynucleotides to detect related sequences or to monitor expression of the corresponding gene constitutes a specific and substantial utility, as defined by the Fisher court. Like the generic utilities asserted in Fisher, Appellants' asserted uses are neither substantial nor specific. Appellants have not disclosed how the results of the asserted hybridization assays would provide a real-world benefit. Thus, just as in Fisher, these uses are "merely hypothetical possibilities, objectives which the claimed [cDNAs], or any [cDNA] for that matter, could possibly achieve, but none for which they have been used in the real world." Fisher, 421 F.3d at 1373, 76 USPQ2d at 1231 (emphasis in original). Therefore, they are not substantial utilities.

Nor are they specific utilities, because they could be asserted for any cDNA transcribed from any gene in the human genome. Because nothing about Appellants' asserted utilities sets the claimed polynucleotides apart from any other human cDNA, Appellants have "only disclosed general uses for [the] claimed [cDNAs], not specific ones that satisfy § 101." Id. at 1374, 76 USPQ2d at 1232.

Appellants also argue that polynucleotides encoding inactive SDHH variants could be used “in assays to detect the presence of metabolism disorders or cancer.”

Appeal Brief, page 5.

This argument is also unpersuasive. The specification states that

Northern analysis shows the expression of SDHH in various libraries, 48% of which are cancerous, 29% are involved in immune response, and 23% are fetal, cell line or proliferating, 22% are from gastrointestinal tissue, 16% from immune tissue, 16% from reproductive tissue, and 12% are from cardiovascular tissue.

Page 15, lines 20-24. (The “Northern analysis” referred to in the quote is not the hybridization assay familiar to those skilled in the art, but an “[a]nalogous computer technique[ ] . . . used to search for identical or related molecules in nucleotide databases.” Specification, page 44.) The specification also states that “SDHH is expressed in tissues which are cancerous, proliferating, or involved in immune response. Therefore, SDHH appears to play a role in disorders of metabolism and cancer.” Page 25, lines 16-18.

The specification, however, provides no explanation for why expression in “tissues which are cancerous, proliferating, or involved in immune response” would suggest that SDHH is involved in “disorders of metabolism.” In addition, the mere fact that SDHH is expressed in cancerous cells does not provide a sufficient basis for asserting that it “play[s] a role in . . . cancer.” Cancer cells are simply normal cells that have lost control over cell division.<sup>5</sup> Thus, the vast majority of proteins expressed by a cancer cell are also expressed by normal cells; the fact that a protein is “expressed in

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<sup>5</sup> See, e.g., Watson et al., Recombinant DNA, 2<sup>nd</sup> edition (1992), page 363 (cancer results when a normal cell sustains a series of mutations that cause it to grow faster) (copy attached).



tissues which are cancerous” is completely inadequate to support an assertion that the protein “play[s] a role in . . . cancer.” The evidence of record does not support the asserted utility of SDHH variants “in assays to detect the presence of metabolism disorders or cancer.”

The uses on which Appellants rely for enablement are not specific and substantial utilities, as required by § 101. We therefore affirm the rejection for lack of enablement.

### 3. Written description

The examiner also rejected claims 3, 6, 7, 9, 11, and 12 under 35 U.S.C. § 112, first paragraph, on the basis that the specification does not provide an adequate written description of the claimed polynucleotides. The examiner acknowledged that the specification discloses one polypeptide having serine dehydratase activity (SEQ ID NO:1, encoded by SEQ ID NO:2) but concluded that the specification does not adequately describe the claimed polynucleotides encoding naturally occurring polypeptides at least 90% identical to SEQ ID NO:2. Examiner’s Answer, page 8.

The examiner reasoned that the structures of the claimed variants is not defined because the level of knowledge in the art does not provide any indication of how the single disclosed species (SEQ ID NO:1) is representative of other naturally occurring variants; thus, the specification’s disclosure does not allow the skilled artisan to envision the structure of the claimed polynucleotides, and a person of skill in the art would not conclude that Appellants were in possession of the claimed invention as of the filing date. Id., pages 8-9.

We agree with the examiner that the instant specification does not describe the claimed genus of polynucleotides that encode “a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1.” The specification discloses the amino acid sequence of SEQ ID NO:1 and one DNA sequence that encodes it (SEQ ID NO:2). That disclosure is adequate to describe all of the DNA sequences that encode the amino acid sequence of SEQ ID NO:1. See In re Wallach, 378 F.3d 1330, 1333, 71 USPQ2d 1939, 1942 (Fed. Cir. 2004) (“[T]he state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it.”).

Claim 3, however, is not limited to polynucleotides encoding the amino acid sequence of SEQ ID NO:1. Appellants also claim polynucleotides encoding “a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1.” That is, the claimed polynucleotides are defined by two characteristics: (1) they are naturally occurring, and (2) they encode amino acid sequences that are at least 90% identical to SEQ ID NO:1.

This appeal does not require us to decide whether the disclosure of an amino acid sequence describes all the DNAs that encode amino acid sequences that are, e.g., 90% identical to the disclosed sequence. For present purposes, however, we will assume that disclosure of SEQ ID NO:1 (which adequately describes all DNAs that encode SEQ ID NO:1) is adequate to describe all DNAs that encode sequences that are 90% identical to SEQ ID NO:1.<sup>6</sup>

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<sup>6</sup> Even if such a genus of DNAs were adequately described, the disclosure of a single amino acid sequence may not be sufficient to enable a skilled artisan to practice the full scope of the genus without undue experimentation. See the discussion of enablement, supra.

The critical question then, is this: assuming that the specification's disclosure is adequate to describe a genus of DNAs (i.e., those that encode sequences at least 90% identical to SEQ ID NO:1), is that same disclosure adequate to describe a subset of those DNAs (i.e., those encoding naturally occurring sequences), even without any disclosure of which members of the large genus are included in the subgenus?

We conclude that describing a genus of chemical compounds is not necessarily adequate to support a claim limited to only those compounds that have a desired characteristic. Rather, the specification must provide guidance regarding which compounds within the genus have the recited characteristic.

The U.S. Court of Appeals for the Federal Circuit, faced with circumstances similar to those here, has held claims to lack adequate description. For example, in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the court held that claims generically reciting cDNA encoding vertebrate or mammalian insulin were not adequately described by the disclosure of cDNA encoding rat insulin. Id. at 1568, 43 USPQ2d at 1406. The court held that

a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. The court described two ways of properly describing a claimed genus:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of

structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. The court has since clarified that the description of representative species does not necessarily have to include their complete structure (nucleotide sequence). See Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002).

The holding of Eli Lilly supports our conclusion that the instant specification does not adequately describe the claimed genus of DNAs – those that encode naturally occurring sequences at least 90% identical to SEQ ID NO:1. The Eli Lilly court held that a fully described genus is one for which a person skilled in the art can “visualize or recognize the identity of the members of the genus.” Here, the specification provides no description of DNAs that encode naturally occurring variants of SEQ ID NO:1 that would allow a person skilled in the art to determine whether a given DNA encoding an amino acid sequence at least 90% identical to SEQ ID NO:1 is within the scope of the instant claims.

The recitation of “naturally occurring” sequences does not imply any structural features that would distinguish the claimed DNAs from non-naturally occurring DNAs. Since the specification does not describe the claimed DNAs adequately for those skilled in the art to distinguish the claimed DNAs from other DNAs, the specification does not adequately describe the claimed DNAs under the standard of Eli Lilly.<sup>7</sup>

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<sup>7</sup> Our conclusion is also consistent with the Eli Lilly court's treatment of claims directed to cDNA encoding human insulin. The court noted that a description that merely renders obvious a claimed invention does not describe that invention adequately to satisfy 35 U.S.C. § 112, first paragraph, and that a claim to a specific DNA is not made obvious by knowledge of the encoded protein sequence and a method of obtaining the DNA. 119 F.3d at 1567, 43 USPQ2d at 1405 (citing Lockwood v. American Airlines, Inc., 107 F.3d 1565, 41 USPQ2d 1961 (Fed. Cir. 1997), and In re Deuel, 51 F.3d 1552, 34 USPQ2d 1210

The court also confronted facts similar to those here in University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004). In that case, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by “administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product in a human.” Id. at 918, 69 USPQ2d at 1888. The patent “described in detail how to make cells that express either COX-1 or COX-2, but not both . . . , as well as ‘assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[.]’” Id. at 927, 69 USPQ2d at 1895.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of which peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims failed to meet the description requirement of § 112. See id. (“As pointed out by the district court, the ‘850 patent does not disclose just ‘which “peptides, polynucleotides, and small organic molecules” have the desired characteristic of selectively inhibiting PGHS-2.’ . . . Without such disclosure, the claimed methods cannot be said to have been described.”).

Just as in University of Rochester, the present application discloses a broad genus of chemical compounds (DNAs encoding amino acid sequences at least 90% identical to SEQ ID NO:1) but the claims are limited to only those compounds having a desired characteristic (encoding naturally occurring sequences). Just as in University of

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(Fed. Cir. 1995)). The Eli Lilly court concluded that “a fortiori, a description that does not render a claimed invention obvious does not sufficiently describe that invention for purposes of § 112, ¶ 1.” Id. The same conclusion logically applies when the claim is directed to a genus of naturally occurring DNA sequences rather than a single naturally occurring sequence.

Rochester, the present specification does not disclose which of the many possible DNAs that encode amino acid sequences at least 90% identical to SEQ ID NO:1 encode naturally occurring sequences.

Granted, those skilled in the art could screen libraries of naturally occurring DNAs to identify for themselves specific DNAs that encode naturally occurring amino acid sequences at least 90% identical to SEQ ID NO:1. That, however, does not make up for the deficiency of the specification's description. The University of Rochester court specifically noted that the patent at issue there disclosed screening assays to identify compounds having the desired characteristic, but nonetheless held that the description was inadequate. The same holds true here.

Appellants argue that the specification discloses SEQ ID NOs 1 and 2, and that “[t]he Specification further describes variant sequences of SEQ ID NO:2 that have at least about 90% identity to SEQ ID NO:2 (specification, page 15, line 33 through page 16, line 7) . . . [and] variants at least 90% identical to SEQ ID NO:1.” Appeal Brief, page 10. Appellants also argue that the “specification also provides guidance in determining percent identity.” Id., page 11. Appellants argue that “the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed.” Id., page 12.

This argument is not persuasive. The cited passage from the specification (pages 15-16) merely recites the same words used in the claims. It does not disclose the structure of any DNAs within the scope of the claim. Further, as discussed above, the court in University of Rochester made clear that § 112 requires a description of

which compounds have the desired characteristic recited in the claims, not simply a description of methods by which those skilled in the art can test compounds to see if they are encompassed by the claims. Because the instant specification provides no description of which DNAs encoding amino acid sequences at least 90% identical to SEQ ID NO:1 encode naturally occurring sequences, the instant specification does not provide the required description.

Appellants also argue that Eli Lilly is distinguishable from the instant case, in that the nucleic acids in that case “were defined on the basis of functional characteristics,” while “the claims at issue in the present application define polynucleotides in terms of chemical structure.” Appeal Brief, pages 12-14.

We are not persuaded by this argument. Although the claimed genus of DNAs is defined in part by structure, it is also defined by the nonstructural characteristic of encoding a naturally occurring amino acid sequence. Thus, the specification must describe the claimed genus sufficiently to allow those skilled in the art to distinguish the claimed DNAs from those that are structurally distinct, and also from those that encode non-naturally occurring amino acid sequences at least 90% identical to SEQ ID NO:1.

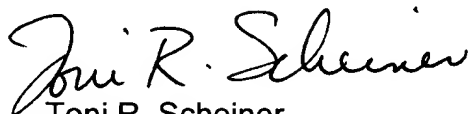
We have considered the other arguments that Appellants raised in response to this rejection but do not find them persuasive. For the reasons discussed above, the rejection of claims 3, 6, 7, 9, 11, and 12 for lack of adequate written description is affirmed.

#### Summary

We affirm the rejection of claims 3-7, 9, 11, and 12 for nonenablement and the rejection of claims 3, 6, 7, 9, 11, and 12 for lack of adequate written description.

No time period for taking any subsequent action in connection with this appeal  
may be extended under 37 CFR § 1.135(a).

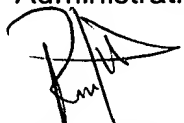
AFFIRMED



Toni R. Scheiner  
Administrative Patent Judge



Eric Grimes  
Administrative Patent Judge



Richard M. Lebovitz  
Administrative Patent Judge

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